REMARKS

Status of the claims

Applicants acknowledge with appreciation the withdrawal of the rejection of claims 17 and 26 under 35 U.S.C § 112, second paragraph, the rejection of claims 18-25, 27 and 28 under 35 U.S.C § 112, second paragraph, the rejection of 17-19, 21-23 and 25 under 35 U.S.C § 103(a) and the rejection of claim 24 under 35 U.S.C § 103(a) in the Office Action dated January 22, 2007.

Applicants have amended claim 17 to recite the adjuvant MF59. New claim 30 has been added and claim 23 has been canceled. Support for the amendments can be found throughout the specification and specifically, on page 2 lines 5-10, 25-30 and page 4 lines 4-6.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Upon entry of the amendments, claims 17-22, 24-28 and 30 are pending in the present application. Claim 23 is presently canceled.

Rejection of Claims 17-19, 21-23 and 25 Under 35 U.S.C. § 103(a)

Claims 17-19, 21-23 and 25 stand rejected under 35 U.S.C. § 103(a) as being unpatenable over Costantino et al. (Vaccine 10: 691-698, 1992) in view of Seid Jr. et al. (US 7,118,757) ('757). This rejection is traversed and believed to be overcome for reasons discussed below.

Specifically, the Office alleges that Costantino et al. disclose a conjugate vaccine comprising immunologically effective amounts of group C meningococcal oliogosaccharides conjugated to CRM 197 and aluminum hydroxide but do not teach the use in their conjugate vaccine of outer membrane vesicles from a strain of group B *Neisseria meningitidis* (Office Action pages 2-3). The Office further notes that Seid et al. ('757) discloses a vaccine formulation comprising OMVs from *Neisseria meningitidis*, including serogroup B *Neisseria meningitidis* strain H44/76 (Office Action page 4). Accordingly, the Office urges that it would

have been *prima facie* obvious to one of ordinary skill in the art to combine Seid Jr.'s ('757) outer membrane vesicle vaccine formulation with Costantino's group C *Neisseria meningitidis* aluminum hydroxide-containing vaccine formulation (Office Action page 5). Applicants respectfully disagree with this assessment.

In order to establish *prima facie* obviousness the following criteria must be met: (1) there must be some suggestion or motivation to modify the references or combine reference teachings; (2) there must be a reasonable expectation of success (for the modification); and (3) the prior art references must teach or suggest all of the claim limitations. Furthermore, the teaching or suggestion and the reasonable expectation of success must both be found in the prior art, not in applicants' disclosure. MPEP §2142. The Office has failed to satisfy these criteria.

Costantino teaches a meningococcus A and C conjugate vaccine. Furthermore, Costantino teaches CRM 197 conjugated meningococcal A and C oligosaccharides with the aluminum hydroxide adjuvant. Costantino does not describe or suggest using such a vaccine with an NmB proteoliposomic vesicle preparation.

Seid Jr. et al. ('757) teaches vaccines comprising isolated OMV's, meningococcal Class 1 OMPs, fragments of OMP and oligopeptides bearing epitopes of the OMP. Seid ('757) also teaches vaccines comprising OMVs from serogroup B *Neisseria meningitidis* strain H44/76. Seid Jr. also suggests the use of an adjuvant, giving specific examples using CFA and alum. Nonetheless, Table 5B depicting MenC-CRM197 conjugate plus alum actually shows data where there is no increased immune response seen with the use of the adjuvant. Specifically, Seid states: "[f]urther, all of the MenC-CB12-10-6 preparations, regardless of adjuvant, elicited antibody response to MenC-HAS..." As such, Seid Jr. et al ('757) does not render the amended claims *prima facie* obvious. Even assuming, *arguendo*, that Seid Jr. et al ('757) provides one of skill in the art with motivation to produce a vaccine formulation with OMVs from serogroup B *Neisseria meningitidis* containing an adjuvant, which it does not, the claims, as amended, include the adjuvant MF59 and thus the reference alone or in combination with Costantino does not provide one of ordinary skill in the art with a reasonable expectation of success.

It is well settled that a patent application can rebut a *prima facie* case of obviousness by a showing of "unexpected results", e.g., by showing that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the art would have found surprising or unexpected. See, e.g., In *re Soni*, 34 U.S.P.Q.2d 1684, 1687 (Fed.Cir. 1995).

In this regard, claims 17-19, 21-23 and 25 are directed to an immunogenic composition comprising a capsular oligosaccharide from serogroup C N. *meningitidis* conjugated to a carrier, proteoliposomic vesicles from serogroup B of N. *meningitidis* and the adjuvant MF59. As explained in examples 2 and 3 of the instant application, the combination of NmB and NmC antigens led to a 2 to 5-fold increase in anti-NmB bactericidal antibody titers, and inclusion of MF59 adjuvant gave the best anti-NmC titers, with antibody response 6-fold greater than those achieved by a "standard" aluminum hydroxide vaccine adjuvant. Thus, applicants discovered, that the combination of NmB outer membrane protein, a conjugated NmC oligosaccharide and a MF59 adjuvant gave a surprisingly effective immune response that was better than the responses achieved with (a) the non-combined antigens or (b) the combined antigens with an aluminum hydroxide adjuvant. See, for example the results presented in Tables 2 and 3.

Based on the cited art, one of skill in the art would not have been led or motivated to produce a vaccine composition comprising NmC conjugated to a carrier with OMVs from NmB and with the adjuvant MF59 with an expectation of success. Moreover, the results provided in the present specification are unexpected.

Accordingly, Applicants submit that claims 17-19, 21-23 and 25 are not obvious in view of each reference alone or when the references are combined.

Rejection of Claim 24 Under 35 U.S.C. § 103(a)

Claim 24 stands rejected under 35 U.S.C. § 103(a) as being unpatenable over Costantino et al. (Vaccine 10: 691-698, 1992) as modified by Seid Jr. et al. (US 7,118,757) ('757), as applied to claim 17, and further in view of Seid (US 6,638,513) ('513). The Examiner acknowledges the combination of Costantino and Sied Jr et al. ('757) does not teach a composition comprising polylactic or polyglycolic acids. Seid ('513) is cited for teaching such carriers. However, the cited combination of references is not believed to render claim 24 obvious. As explained above, claims 17-19, 21-23 and 25 are directed to an immunogenic composition comprising a capsular oligosaccharide from serogroup C N. *meningitidis* conjugated to a carrier, proteoliposomic vesicles from serogroup B of N. *meningitidis* and the adjuvant MF59. Seid ('513), when applied to this combination, does not supply the missing elements. Seid ('513) teaches the use of polylactic or polyglycolic acids in combination with meningococcal oligosaccharide derivatives.

None of the cited art teach or suggest an immunogenic composition comprising a capsular oligosaccharide from serogroup C.N. *meningitidis* (NmC) conjugated to a carrier with proteoliposomic vesicles from serogroup B of N. *meningitidis* (NmB) and the adjuvant MF59. Moreover, the results provided in the present specification are unexpected. Accordingly, claims 17-19, 21-23 and 25 are not obvious in view of Seid Jr. et al. ('757). Furthermore, claim 24 is not obvious in view of Seid ('513) or in view of Costantino as modified by Seid ('513). Reconsideration and withdrawal of the rejection of claims 17-19, 21-25 under 35 U.S.C. § 103(a) is requested.

If further fees are due, the Commissioner is hereby authorized to charge any deficiencies to deposit account number 03-1664 to facilitate the filing of this application. However, this is not authorization to charge the Issue Fee.

Correspondence

Please direct all further communications regarding this application to:

Amy Hessler
Novartis Vaccines and Diagnostics, Inc.
Intellectual Property – R440
P.O. Box 8097
Emeryville, CA 94662-8097
Telephone: (510) 923-3833
Facsimile: (510) 655-3542.

Respectfully submitted,

NOVARTIS VACCINES AND DIAGNOSTICS, INC.

By: _____

Amy Hessler
Registration No. 50, 310
Telephone: (510) 923-3833
Facsimile: (510) 655-3542

Emeryville, CA 94662-8097
Dated: 6/15/07